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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,220	12/04/2006	Craig B. Thompson	130694.01201	4279

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EXAMINER	
LOVE, TREVOR M	

ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
05/05/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/556,220	THOMPSON ET AL.	
	Examiner	Art Unit	
	TREVOR LOVE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-10,12-16,20,21,36,49-51,64,65,68-72,75-77 and 79-99* is/are pending in the application.

4a) Of the above claim(s) *9 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,10,12-16,20,36,49-51,64,65,68-72,75-77 and 79-99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/25/2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/25/2011 has been entered.

Acknowledgement is further made to Applicant's supplemental response filed 04/27/2011

Claims 1-6, 8-10, 12-16, 20, 21, 36, 49-51, 64, 65, 68-72, 75-77, and 79-99 are pending.

Claims 9 and 21 are withdrawn.

Claims 16, 20, and 21 are currently amended.

Claims 75-77 and 79-99 are newly added.

Claims 1-6, 8, 10, 12-16, 20, 36, 49-51, 64, 65, 68-72, 75-77, and 79-99 are currently under consideration.

Note: Applicant's election of record includes:

Invention I (claims 1-26, 35-37, and 49-53);

Glioblastoma cells as the cancer cell species;

Hydroxycitrate as the ATP citrate lyase inhibitor species;

Phosphoenolpyruvate as the tricarboxylate inhibitor species.

Withdrawn Rejections and/or Objections

The rejection of claims 52, 58-63, and 74 under 35 U.S.C. 103(a) as being unpatentable over Kuhajda et al. (US Patent 5,759,837, Patent issued Jun. 2, 1998), in view of Schroder et al. (1999, Int. J. Gynecol Cancer) is withdrawn in view of Applicant's cancellation of said claims.

The rejection of claims 17-19, 52, 58-63, 66, 67, 73, and 74 under 103(a) as being unpatentable Kuhajda et al. (US Patent 5,759,837, Patent issued Jun. 2, 1998), in view of Schroder et al. (1999, Int. J. Gynecol Cancer) as applied to claims 1-6, 8, 10, 12-15, 50-52, 58-65, 68-72, and 74, and further in view of Bru et al. (US Patent 5,219,846, Patent issued Jun. 15, 1993) is withdrawn in view of Applicant's cancellation of said claims.

Pending Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 8, 10, 12-15, 20, 50, 51, 64, 65, 68-72, 79-85, and 87-99 rejected under 35 U.S.C. 103(a) as being unpatentable over Kuhajda et al. (US Patent 5,759,837), in view of Schroder et al. (Int. J. Gynecol. Cancer).

Kuhajda teaches methods of treating carcinomas comprising administering a compound that inhibits fatty acid synthase (FAS), including inhibitors of citrate lyase such as hydroxycitrate (see Abstract, column 3, line 52-54 and column 11, lines 22-34 and 60). Kuhajda teaches that since many tumor cells are extremely dependent on endogenous fatty acid synthesis, lower FAS activity levels need not exclude a specific tumor as a candidate for therapy with fatty acid synthase inhibitors (see column 7, lines 61-64). Kuhajda teaches that it is advantageous to combine the active of Kuhajda with chemotherapeutic agents to target rapidly cycling cells (see column 8, lines 53-65).

Kuhajda teaches that the presence of FAS in cells of the carcinoma may be detected by any suitable method, including activity assays, stains, and immunoassays (see column 7, line 65 to column 8, line 22).

Kuhajda fails to directly teach that the cancer is identified as comprising cancer cells that have a high rate of aerobic glycolysis, that said cancer is identified by PET imaging utilizing ^{18}fluroro-deoxyglucose (^{18}F-FDG), or that said cancer is glioma.

Schroder teaches the role of ^{18}F-fluoro-deoxyglucose positron emission tomography (^{18}F-FDG PET) in diagnosis of cancer. Schroder states that the clinical significance and usefulness of PET has been proven for a variety of malignant tumors, and specifically names glioma (see page 117, columns 1 and 2). Schroder teaches that "[i]n 1931 Warburg demonstrated that malignant tumors are characterized by an elevated aerobic and anaerobic glycolysis" (see page 117, first sentence).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the ^{18}F-FDG PET imaging as taught by Schroder to diagnose a patient with cancer for treatment with the composition of Kuhajda. One would have been motivated to do so since Schroder teaches that ^{18}F-FDG PET imaging is useful in diagnosing malignant cancers, which, according to Warburg as cited by Schroder, necessarily comprises elevated aerobic glycolysis. There would be a reasonable expectation of success in utilizing the diagnostic method of Schroder to diagnose a carcinoma which is to be treated with the composition of Kuhajda since Kuhajda teaches that the carcinoma may be detected by any suitable method (see Kuhajda, column 7, line 65 to column 8, line 22).

It would further have been obvious to one of ordinary skill in the art at the time the invention was made to treat a cancer patient with a FAS inhibitor and a different chemotherapeutic agent or radiation therapy to control tumor growth. One would have been motivated to do so because Kudhajada suggest that FAS inhibitors may be utilized in conjunction with other therapeutic programs, wherein Kudhajada states that chemotherapy and radiation therapy are the most common forms of tumor treatment (see column 1, lines 36-43 and column 8, lines 58-65).

With regard to the newly added limitations directed to Akt and PTEN, it is noted that Applicant's elected species of cancer is glioma, wherein Applicant identifies that the newly added claims read on the elected species. Therefore, said glioma would have said identified characteristics associated with Akt and PTEN.

Response to Arguments

Applicant argues in the remarks filed 04/25/2011 that "Nothing in Kuhajda teaches or suggests that in treating cancer, cancer cells which have a high rate of glycolysis are more sensitive to treatment with citrate lyase" (see remarks, page 13, also, similar argument page 14). Applicant argument is not found persuasive since Kuhajda in view of Schroder renders obvious the instantly claimed method, and as such, the art is not required to teach the same reasoning for adding components as Applicant, MPEP 2144 (IV) states "the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by Applicant. See, e.g., *In re Kahn*,

411 F.3d 977, 987, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)." Applicant further states that "Kuhajda does not recognize the link between cancer cell which exhibit elevated levels of glycolysis and the use of citrate lyase inhibition to induce apoptosis in cancer cells displaying such a metabolic profile" (see remarks, page 13). Applicant's argument is again not found persuasive since the method of Kuhajda in view of Schroder would result in the same patient population receiving the same treatment, therefore, Applicant's argument is not persuasive. Applicant further argues that "PET does not image all tumors, only those with elevated rates of glycolysis compared to adjacent tissue (see remarks, page 14). Applicant's argument is not persuasive to overcome the instant rejection since sufficient motivation exists in the prior art to utilize the PET imaging of Schroder in the invention of Kuhajda. As such, Applicant's argument is not found persuasive.

Claims 16, 36, 49, and 75 are rejected under 103(a) as being unpatentable Kuhajda et al. (US Patent 5,759,837), in view of Schroder et al. (Int. J. Gynecol Cancer) as applied to claims 1-6, 8, 10, 12-15, 20, 50, 51, 64, 65, 68-72, 76, 77, and 79-99 above, and further in view of Bru et al. (US Patent 5,219,846).

The teachings of Kuhajda and Schroder are set forth above.

Kuhajda, while teaching that FAS inhibitors (e.g. ATP lyase inhibitors) can be combined with other chemotherapeutic agents, fails to directly teach that the composition further comprises a tricarboxylate transporter inhibitor, namely phosphoenolpyruvate (elected species).

Bru teaches methods for treating human tumors; particularly tumors that have become resistant to chemotherapy comprising administering an effective amount of phosphoenolpyruvic acid (see Abstract and column 1, lines 41-64).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the phosphoenolpyruvic acid of Bru with the citrate lyase inhibitor (e.g. hydroxycitrate) of Kuhajda for additive anti-tumor effects. One would have been motivated to do so since Kuhajda teaches that FAS inhibitors (e.g. ATP lyase inhibitors) can be combined with other chemotherapeutic agents and phosphoenolpyruvic acid as taught by Bru is a chemotherapeutic agent. It is further noted that MPEP 2144.05 states: ""It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); and *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992).

Response to Arguments

Applicant argues in the remarks filed 04/25/2011 that the teachings of Bru do not cure the deficiencies identified above for Kuhajda and Schroder. Applicant's arguments are not found persuasive since the alleged deficiencies are not found persuasive as identified above. Applicant further argues that PET is one of several methods that can be used to identify a tumor, where none of the references teach using PET for the same

reason as Applicant. Applicant's argument is not found persuasive. Specifically, the art is not required to teach the same reasoning for adding components as Applicant, MPEP 2144 (IV) states "the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by Applicant. See, e.g., *In re Kahn*, 411 F.3d 977, 987, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)."

Claims 76, 77, and 86 are rejected under 103(a) as being unpatentable Kuhajda et al. (US Patent 5,759,837), in view of Schroder et al. (Int. J. Gynecol Cancer) as applied to claims 1-6, 8, 10, 12-15, 20, 50, 51, 64, 65, 68-72, 76, 77, and 79-99 above, and further in view of Brin et al. (US PreGrant Publication number 2002/0094339).

The teachings of Kuhajda and Schroder are set forth above.

Kuhajda, while teaching that FAS inhibitors (e.g. ATP lyase inhibitors) can be combined with other chemotherapeutic agents, fails to directly teach that the composition further comprises an antibody.

Brin teaches that chemotherapeutics which are most commonly used include antitumor antibodies, and namely Herceptin (see entire document, for instance, [0024]). It is noted that herceptin is the only example of an antibody provided in the instant specification (see specification, page 12, lines 13-14).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the herceptin of Brin with the citrate lyase inhibitor (e.g. hydroxycitrate) of Kuhajda for additive anti-tumor effects. One would have been motivated to do so since Kuhajda teaches that FAS inhibitors (e.g. ATP lyase inhibitors) can be combined with other chemotherapeutic agents and herceptin as taught by Brin is a common chemotherapeutic agent specifically taught as being anti-tumor. It is further noted that MPEP 2144.05 states: ""It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); and *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992).

Conclusion

No claims allowed. All claims rejected. No claims objected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TREVOR LOVE whose telephone number is (571)270-5259. The examiner can normally be reached on Monday-Thursday 7:30-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TL

/Lakshmi S Channavajjala/
Primary Examiner, Art Unit 1611